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Review Article

Anesthetic Approach to Hepatectomy: A Literature Review

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Summary

Hepatectomy is considered a major abdominal surgery, with potential complications, especially in patients with chronic liver disease. In this article, we explore the anesthetic approach in liver surgery, from pre-anesthetic assessment to strategies for reducing bleeding and fluid resuscitation. Anatomical considerations are crucial to avoid complications, given the hepatic complexity. During surgery, constant monitoring of pulse pressure variation (Delta PP) and Central Venous Pressure (CVP) provides information about blood volume and cardiovascular function. Different anesthetic techniques, such as epidural, general anesthesia and erector spinae plane block, should be considered according to the surgery and the patient. In short, a well-planned anesthetic approach is essential to optimize surgical results and ensure patient safety in challenging liver surgeries. This article aims to provide a comprehensive synthesis of the critical steps in the anesthetic approach to liver surgery.

Keywords: Anesthesia; General surgery; Hepatectomy; Liver

Introduction

The liver has the unique ability to regenerate its functional tissue after tissue loss. This physiological characteristic has been fundamental for the development of liver resection surgery, which has become a common procedure today. In the past, in the 1970's, perioperative mortality for liver resection reached approximately 20%, mainly due to problems such as uncontrolled bleeding and liver failure after surgery. However, significant advances in the understanding of liver anatomy, careful patient selection and the improvement of surgical and anesthetic techniques have contributed to a significant reduction in perioperative mortality, currently around 3%. It is important to note that patients with parenchymal liver diseases, such as cirrhosis, still have higher rates of complications and mortality, which demands a careful approach in these cases [1].

The anesthetic approach to liver surgery is complex and multifaceted, involving steps from the pre-operative period to post-surgical recovery. Due to the liver's rich vascularization, pre-anesthetic evaluation is crucial, especially for patients with liver disease. Liver dysfunction can affect the metabolism of anesthetics and medications, while risks such as heart failure and compromised gas exchange need to be evaluated. During surgery, the risk of bleeding is considerable, requiring anesthetic strategies to maintain hemodynamic stability and control coagulation. Collaboration between medical teams is essential to face bleeding complications. Prevention of hypothermia and correction of intraoperative coagulopathy are equally vital. In summary, a successful anesthetic approach to liver surgery depends on an in-depth understanding of liver anatomy, interdisciplinary collaboration, and thorough considerations that span all phases of the procedure [2,3].

Anatomic Considerations

The liver is a highly vascularized organ, receiving a total blood flow of 1.5 liters per minute. This blood supply is distributed mainly through the portal vein, which supplies around 80% of the blood, and the hepatic artery, responsible for the remaining 20%. In anatomical terms, the liver can be divided into five sectors, which, in turn, are subdivided into eight functional segments, each described according to its blood supply and biliary drainage, as shown in (figure 1). The portal vein branches successively to supply each hepatic segment, presenting similar divisions in the hepatic arteries and bile ducts. The peculiarity of blood supply and biliary drainage in distinct segments allows adjacent segments to be resected without interrupting the vascular supply of neighboring tissues. This special anatomy provides a dissection with little bleeding and a functional division that is not easily visible on the surface of the liver [2].

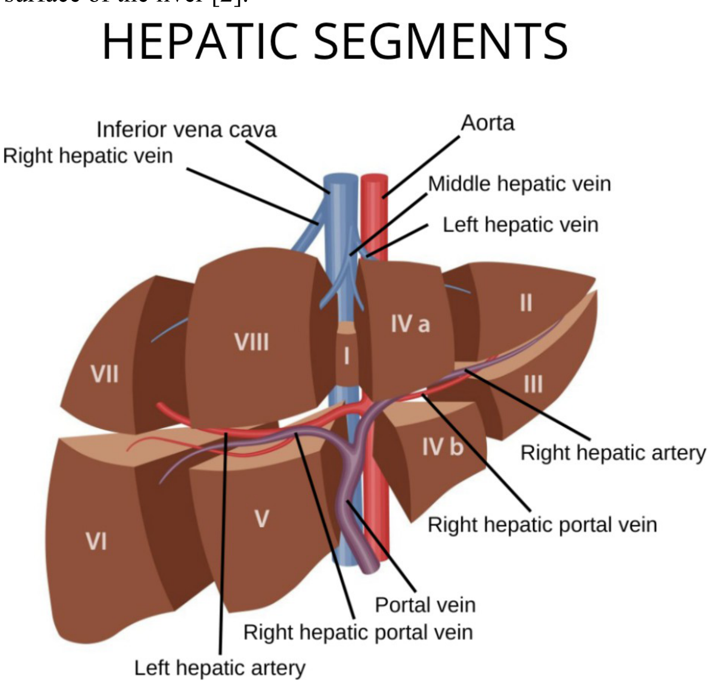

Figure 1: Liver anatomy by hepatic segments.

Surgical Technique

The primary objective of surgical intervention is to perform precise excision of the affected part of the liver, ensuring complete removal of oncologically relevant components. Minimizing blood loss is essential, while preserving a healthy portion of the liver to prevent liver failure and enable the regeneration process. Laparoscopic surgery is the method of choice, according to scientific literature, as it presents advantages, such as less postoperative pain and lower risk of bleeding. Occasionally, an additional incision may be necessary, manually assisted by a gas-tight glove, to optimize the execution of the procedure [4].

The surgical approach can be divided into three main phases: the initial preparation phase, resection of the affected tissue, and confirmation of hemostasis and careful closure of the surgical wound. In the preparation phase, the liver tissues connected to the peritoneum are displaced, in addition to proceeding with cholecystectomy and, if necessary, the hepatic vascular anatomy is exposed. As for the resection phase, there are numerous possible surgical techniques, but the general principle is resection of the liver parenchyma with ligation of the vessels and bile ducts. At this stage, to reduce blood loss, there is a temporary clamping of the vessels responsible for the hepatic blood supply (portal vein and hepatic artery), known as the “Pringle maneuver”, which ends up interfering with the patient’s hemodynamics, through a drop in blood flow. Heart rate and increased cardiac afterload. The last step consists of confirming hemostasis and closing the abdominal wall. Each step is crucial to ensure the effectiveness of the procedure and the patient’s recovery [1,4].

Pre-Anesthetics Assessment

Preoperative assessment should be tailored to the needs of each individual patient, based on general comorbidities and liver failure. Patients without parenchymal liver disease are evaluated for any major intra-abdominal operation. However, patients with liver disease are at significantly increased risk of multiple organ failure, including heart failure, impaired gas exchange, bleeding, and renal failure, warranting further evaluation. This may include pulmonary function testing, arterial blood gas analysis and echocardiography. A significant number of patients presenting for resection of liver metastases will have received neoadjuvant chemotherapy, which can reduce cardiac reserve function. Of particular concern are conditions that cause an elevation in right cardiac and central venous pressure (CVP) that significantly increases the risk of intraoperative bleeding. Early communication with the surgical team will identify cases at high risk of intraoperative bleeding, extensive resection, or liver failure. Patients with hepatic carcinoid present a particular challenge, but the safety of these resections has been greatly improved with the use of octreotide (Table 1) [5,6].

In young patients (up to 40 years old) with normal liver parenchyma, the literature indicates that it is safe to remove up to four liver segments, totaling a resection of 50 to 60%, although survival after resection of 80% is possible [3]. However, occasionally patients develop significant postoperative liver failure after apparently safe resections, especially in alcoholic patients. Currently, there is no single test that reliably predicts postoperative liver failure, and assessment is made based on laboratory and radiological investigations, quantitative tests, and surgical judgment [1,3,6]. Thorough analysis of liver function plays an important role, especially given the prevalence of underlying liver diseases, such as cirrhosis or hepatic steatosis, among patients undergoing this type of procedure. The assessment of liver function involves carrying out tests to measure parameters such as serum levels of bilirubin, albumin, prothrombin time (PT) and international normalized ratio (INR). These tests provide vital information about the liver's ability to synthesize clotting proteins, in addition to evaluating its metabolic and detoxification function.

The Child-Pugh clinical scoring system (Table 2) has been used as a reliable and validated prognostic tool for patients with liver disease; it has recently been suggested that patients with a score of B or C should not receive liver resection surgery [7]. C Patient Blood Management (PBM) plays an important role in preparing for liver surgery. The method is evidence-based, with the goal of maintaining hemoglobin concentration, optimizing hemostasis, and minimizing blood loss in an effort to improve patient outcomes [8]. Maintaining adequate hemoglobin levels before surgical intervention is essential to ensure a sufficient blood reserve during the procedure, thus reducing the need for intraoperative transfusions. This is particularly relevant in liver surgery, where the risk of blood loss is significant [9]. Strategies such as iron supplementation, administration of erythropoiesis-stimulating agents and optimization of cardiovascular health can contribute to raising hemoglobin levels and, consequently, improving perioperative results. Preoperative hemoglobin management not only minimizes the risks associated with perioperative anemia but also promotes faster and more effective recovery after liver surgery [8,9].

Specific strategies are adopted to optimize the management of patients with liver disease and hemostatic abnormalities before and during liver surgery. In patients with elevated prothrombin activity time, preoperative administration of vitamin K is a common practice [10].

When it comes to patients at risk of bleeding, whether due to microvascular bleeding or percutaneous procedures, both in the preoperative and intraoperative periods, platelet administration is indicated to maintain a count, on average, above 50,000/microL. Furthermore, cryoprecipitates can be used to ensure fibrinogen levels above 200 mg/dL [11]. Administration of fibrinogen concentrate may also be considered for this purpose. Administration of fresh frozen plasma to correct INR is not routinely done. It is important to highlight that patients with liver disease may present a prothrombotic profile, even with altered conventional coagulation tests (TAP and APTT) [6].

In settings where viscoelastic tests, such as thromboelastography (TEG) or thromboelastometry, are available, these tools prove useful in guiding the correction of hemostatic abnormalities in patients with liver disease. One study in particular demonstrated that TEG guidance reduced the need for blood product transfusions in patients with cirrhosis and significant coagulopathy, without increasing the risk of bleeding complications [12].

Preanesthetic evaluation	• Surgery in patients with Child-Pugh score B or C should be reconsidered • Preoperative examination: ○ complete blood count ○ coagulation tests ○ glycemic profile ○ renal function ○ electrolytes • Reserve at least: ○ 02 red blood cell concentrate
Useful Advanced Monitoring	• Central Venous Pressure • Pulse pressure variation (Delta PP) • Conscious monitoring • Cardiac output monitor
Anesthetic technique	• General, associated to: ▪ Peridural or ▪ ESPB bilateral • Catheter maintenance in the postoperative period is advantageous

Position	• Supine
Duration	• 2-6 hours (depending on the surgeon's experience and the complexity of the surgery)
Bladder catheterization	• Required • Urine output must be maintained >0.5 mg/kg/hr
Estimated Blood Loss	• 250-1000 mLs (correlated to PVC)
Heating recommendations	• Hypothermia worsens enzymatic activity and coagulation • Central thermometer • Heated solutions • Heating mantle
Volume replacement	• Restricted pre-resection • Buffered solution is the preferred crystalloid • Albumin is the preferred colloid when indicated (resections > 40%)
Invasive Blood Pressure	• Recommended
Peripheral Venous Acess	• 02 caliber accesses
Central Venous Acess	• Common use
Vasodilators	• Nitroglycerin can be used to reduce PVC
Measures to reduce blood loss	• Maintain CVP < 5 cmH2O • Restricted volume replacement • Vasodilators use • Antifibrinolytics use • Maintenance of hemostasis factors • Intermittent Pringle Maneuver (Surgeon)

Table 1: Anesthesic considerations in hepatectomy.

Child-Pugh Classification			
Hepatic encephalopathy	None	1-2	3-4
Ascites	None	Mild	Moderate to severe
Albumine (g/dL)	> 3,5	2,8-3,5	< 2,8
Total bilirrubine (mg/dL)	> 2,0	2,0-3,0	> 3,0
INR	< 1,7	1,7-2,3	> 2,3
Points:	1	2	3
A: 5-6 points	B: 7-9 points		C: 10-15 points

Table 2: Child-Pugh classification.

Perioperative Monitoring

The monitoring technique must respond to all risks of the procedure: cardioscopy, oximetry, esophageal temperature and monitoring of consciousness with BIS must be used. It is recommended to obtain central venous access for rapid infusion of blood concentrates and vasopressors. The use of invasive blood pressure and dynamic measurements of cardiac output and pulse pressure variation has progressively replaced the use of pulmonary artery catheters due to their lower morbidity and similar effectiveness in helping the anesthesiologist manage fluid responsiveness. Furthermore, for better hemodynamic control, especially in moments of vascular occlusion, central venous pressure (CVP) is suggested [3].

Due to the high possibility of bleeding during the surgical procedure, one must be aware and prepared for this possibility. Checking for possible hypoglycemia, using blood glucose, is of fundamental importance, given the possibility of its occurrence, especially during the period of vascular clamping. Body temperature must be checked during the procedure, as hypothermia can cause hemodynamic and coagulation changes [3].

There is also a need to check intraoperative coagulation parameters, which can be influenced by several factors, such as acidosis, hypocalcemia and hypothermia, for example. Such monitoring is carried out through laboratory tests and, if correction is necessary, an infusion of fresh frozen plasma must be performed. Other devices that can be used, depending on the availability of the service, are the pulmonary artery catheter (Swan-Ganz) and transesophageal echocardiography. The latter should be used with caution due to the possibility of bleeding secondary to esophageal varices or active coagulopathy. Therefore, it is recommended to avoid passing the transgastric transducer, in order to avoid further esophageal manipulation. However, despite this, the rate of complications, bleeding and gastroesophageal injuries is very small compared to its benefit [13,14].

Another extremely important factor in intraoperative monitoring is the variation in pulse pressure (delta PP), which can indirectly show the efficiency of cardiac output, in addition to evaluating the response to fluid therapy and patient's volume status. Pulse pressure consists of the difference between systolic pressure and diastolic pressure, therefore, the greater their difference, the greater the patient's cardiac output. Intraoperative fluid administration after anesthetic induction can be based on delta PP. When its value is between 10 and 20%, 3 to 4 mL/kg/h must be infused until the hepatectomy is completed. As long as it has values below 10%, it must be infused at a rate of 2 mL/kg/h, and diuretics can be administered to better control Δ PP. After the procedure is completed, a crystalloid or colloid solution (albumin) must be infused at a rate of 8 to 10 mL/kg/h. Such perioperative infusion management is in the algorithm in (Figure 2) [15,16].

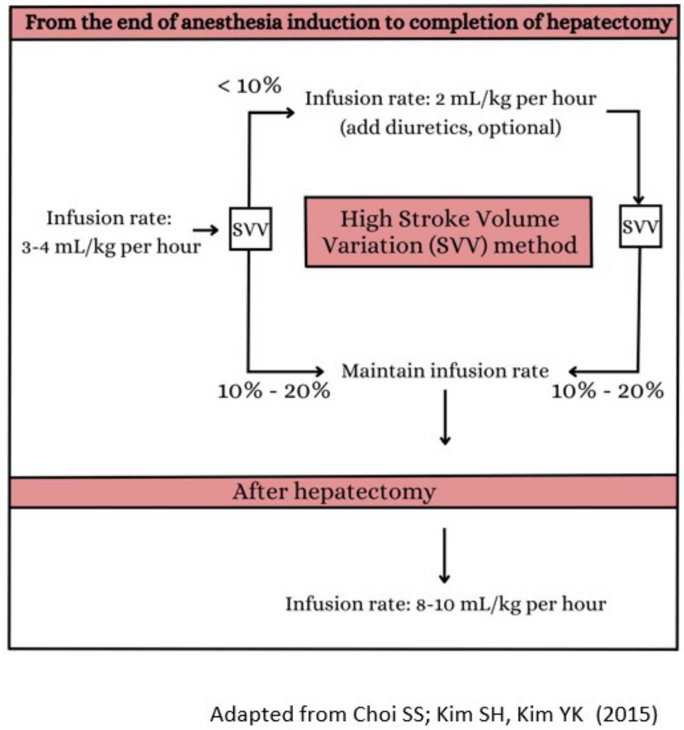

Figure 2: Algorithm of stroke volume variation-guided fluid management during hepatectomy.

Anesthetics Technique

Optimal anesthetic management for any surgery is based on understanding the patient and their disease as a whole, including the risks of each procedure. In hepatectomy, the constant concern with changes in the functioning of the liver parenchyma presents itself as a challenge that requires specific care for each patient.

The use of general anesthesia is mandatory. Due to the intense abdominal manipulation and the risk of significant bleeding through adjacent vascular structures, airway patency and the patient's unconsciousness must be guaranteed. Anesthesia can be maintained with inhaled or intravenous drugs. The use of halogenated drugs allows titration that does not depend on liver function; however, some of the older classes present a risk of hepatotoxicity. On the other hand, intravenous anesthetics have a more complex titration due to changes in hepatic metabolism resulting from the procedure, increasing the risk of intraoperative memory.

Although general anesthesia is a standard practice, other methods are usually combined with it, such as regional and neuraxial blocks, aiming for better intra- and postoperative analgesic control. This concern is essential, as the incisions in open hepatectomy are relatively large, such as the bilateral subcostal (chevron incision), with possible medial extension (Calne or Mercedes-Benz incision) [17].

Performing techniques combined with the use of neuraxial blocks or regional blocks presents advantages when we consider the need for rapid recovery in this population, which has an increased risk of perioperative thrombosis [18]. The use of an epidural, often considered the gold standard in major abdominal manipulation surgeries, raises concern due to the possibility of hematoma formation in this region, since it is uncertain whether the patient's coagulation profile will change after the attacks resulting from the procedure. Therefore, this is the main determinant in choosing the anesthetic block that will be performed.

Among the strategies that can be used, a relatively recent technique also stands out, the Erector Spinae Plane block (ESP block). This approach involves administering local anesthetic between the erector spinae muscles and the fascia that covers them. The anesthetic diffuses into this space, providing effective analgesia to the surgical area and neighboring regions. The advantages are significant, as analgesia is provided not only in the direct area of application, but also in adjacent areas, thanks to the diffusion of the anesthetic. It is often assisted by ultrasound for precise guidance. One of the main advantages is the reduction in the need for postoperative opioids due to the effective analgesia offered by the block, minimizing its potential side effects. However, it is important to note that its effectiveness may vary between patients. In some cases, it may not provide the same desired level of analgesia [19].

During hepatectomy, where occlusion of the portal triad inflow is a common approach to minimize blood loss, there is significant concern about possible ischemia-reperfusion injury to the remaining portions of the liver. In this context, dexmedetomidine, an alpha-2 adrenergic agonist, has emerged as an additional strategy to mitigate the adverse effects of ischemia-reperfusion. Dexmedetomidine plays a crucial role in reducing ischemia-reperfusion injury, which can be evidenced by the results of a recent prospective, randomized and controlled study. In this study, patients undergoing hepatectomy were divided into two groups: one group received dexmedetomidine and the other acted as a control group. Assessments included serum markers such as albumin, aspartate aminotransferase and alanine aminotransferase, as well as prothrombin time. Notably, patients in the dexmedetomidine group had lower levels of these markers, suggesting a reduction in liver injury. Furthermore, the duration of hypotension was shorter in the dexmedetomidine group, indicating better hemodynamic control. The study group also demonstrated a reduced need for vasopressors, less blood loss, and less use of colloids, crystalloids, and blood transfusions compared to the control group. Taken together, these findings highlight that dexmedetomidine offers effective liver protection during hepatic resection surgeries with portal inflow occlusion, contributing to minimizing blood loss and reducing the need for transfusions.

Volume Replacement

Volume replacement is of fundamental importance in the treatment of hypovolemia, frequently observed in the perioperative period, especially in hepatectomies, as well as in seriously ill patients. The objective of fluid administration is to restore tissue perfusion, ensuring adequate blood flow to vital organs and preventing complications related to hypovolemia. Although isotonic solutions have traditionally been used for this purpose, their results have not always been satisfactory, especially in cases of severe shock. Regardless of the type of shock, the common outcome is widespread tissue perfusion failure.

A wide variety of fluids can be used for volume replacement. Options include crystalloid solutions, plasma, albumin and synthetic colloidal solutions such as gelatins, dextran and, more recently, hydroxyethyl starch. The choice between these fluids often takes into account the sodium concentration and oncotic pressure of each solution. Isotonic crystalloid solutions, such as lactated Ringer's and saline solution, have a sodium concentration similar to that of plasma, but do not have oncotic pressure due to the lack of proteins.

The liver plays a crucial role in the metabolism of organic anions, consuming hydrogen ions and regenerating the extracellular bicarbonate buffer. These anions can be exogenous, such as citrate in blood transfusions, or endogenous, including lactate from glycolysis or anaerobic metabolism. During hepatectomy, hepatic metabolism can be impaired, affecting the ability to metabolize organic anions present in administered solutions, compromising the generation of bicarbonate [15,20].

The use of an acetate buffer in hepatectomies is theoretically advantageous over a lactate buffer. While crystalloid solutions with lactate can lead to hyperlactatemia due to liver failure, the acetate anion is metabolized in muscles and organs, not depending on the liver. Furthermore, it is more alkaline and is metabolized more quickly than lactate, increasing bicarbonate levels within 15 minutes of administration, bringing greater benefit [9].

More recent literature demonstrates that fluid resuscitation with balanced solutions, such as Plasma-Lyte, in critically ill patients has demonstrated more biochemical stability and hematological profiles when compared to saline or lactated Ringer's. The fastest normalization of hyperchloremia and acidosis occurred with acetate. Furthermore, acetate is age-independent and can prevent malnutrition by acting as a fat substitute without affecting glucose homeostasis. On the contrary, the administration of lactate solutions can cause hyperglycemia in diabetic patients. These aspects highlight the potential of using acetate in hepatectomies [20].

Albumin is a protein produced by the liver, which plays an important role in maintaining osmotic pressure and water-electrolyte balance in the body. It also transports hormones, drugs and other substances in the blood. In patients undergoing hepatectomy, albumin can be used to replace blood volume and prevent complications such as hypotension, edema, ascites and renal failure. It can also improve liver function and heal remaining tissue.

Indications for the use of albumin for volume replacement in hepatectomy depend on several factors, such as the extent of hepatectomy, presence of cirrhosis, preoperative serum albumin, oncotic pressure and hemodynamic status. In general, the use of albumin is recommended in liver resections in which more than 40% of the liver is removed and in liver transplants, especially in cases of ascites and edema in the postoperative period, when serum albumin is less than 2.5 g. Osmotic pressure below 12 mmHg.

The dose and duration of albumin infusion should be adjusted based on the patient's weight, clinical condition, and laboratory parameters. Furthermore, caution should be exercised in patients with heart failure, hypertension, anemia, or protein allergies [20].

Strategies to Reduce Intraoperative Bleeding

Blood loss of more than 10 liters has been reported following liver resection surgeries, and large transfusions are associated with significant risks of serious postoperative complications and liver failure. Patients with cirrhosis, steatosis and after chemotherapy face an increased risk of coagulopathy and bleeding. However, modern and multimodal perioperative approaches have contributed to reducing the average blood loss to a range between 300 and 900 ml. Although the use of intraoperative cell salvage is a controversial practice in malignant surgeries, blood optimization techniques have evolved [3].

Low Central Venous Pressure (CVP)

Low Central Venous Pressure (CVP) plays a crucial role during parenchymal resection as reflux from valveless hepatic veins is the main source of bleeding. Control of central and hepatic CVP is essential to minimize blood loss. Studies document that a CVP above 5 cmH2O is associated with a significant increase in bleeding. However, maintaining a low CVP presents risks such as cardiovascular stability, hypovolemia, air embolism and reduced renal blood flow. However, the potential theoretical risk of postoperative renal dysfunction does not demonstrate clinical importance. Some patients require a CVP of 5 cmH2O for cardiovascular stability, and in such cases, an individualized compromise must be reached. Hypotension after induction, especially with the use of epidural anesthesia, can be treated initially with head-down tilt and infusions of vasoconstrictors such as phenylephrine or a low-dose inotrope such as dobutamine (3 mg/kg/min) of in order to avoid volume infusion and consequently an increase in CVP. Pre-resection fluid administration should be restricted, although colloid boluses may be appropriate if urine output is less than 0.5 ml/kg/h or in the case of refractory hypotension. Elevated CVP can be controlled with diuretics or nitrate infusion. After the resection phase, circulating blood volume can be restored, as although the risk of bleeding remains, it is considerably reduced [3,6].

Antifibrinolytics

It is known that the liver is the organ responsible for the synthesis of coagulation inhibitors, fibrinolytic proteins and their inhibitors, in addition to all coagulation factors, with the exception of Von Willebrand factor. Therefore, more complex bleeding management is expected in patients with active liver damage [6].

Therefore, the use of antifibrinolytics is an effective tactic to reduce bleeding in liver surgical procedures. These pharmacological substances act by inhibiting the premature dissolution of blood clots, preventing excess fibrinogen degradation and stabilizing the coagulation process.

The administration of antifibrinolytics has shown success in reducing intraoperative blood loss, especially in surgeries with high hemorrhagic risk. By preventing hyperfibrinolysis induced by surgical trauma, these agents help maintain hemostasis, which results in less need for blood transfusions and minimization of risks associated with considerable blood loss.

Tranexamic acid is a synthetic analogue of lysine. Its dosing schedule for hepatectomies follows the group for non-cardiac surgeries in patients at high risk of bleeding. The proposal is an intravenous bolus of 10-15 mg/kg before the first incision followed by 1-2 mg/kg/h continuous infusion until the end of the surgery. In patients with a lower convulsive threshold or underlying renal dysfunction, aminocaproic acid appears to be a more appropriate option [21]. Its regimen involves a loading dose of 5 to 10 g (or 75 to 150 mg/kg), followed by 1 g/hour (or 10 to 15 mg/kg/hour) until the end of the procedure or up to 8 hours after the procedure.

However, it is imperative to carefully consider the administration of these medications, evaluating each patient's particularities, drug interactions and potential side effects, in order to ensure an adequate balance between efficacy in reducing bleeding and perioperative safety.

Postoperative Care Related to Bleeding

Although an increase in liver enzymes in the postoperative period is common, especially in surgeries related to the upper abdomen, a limit of twice the normal value increase is stipulated to assume that an active hepatocellular lesion is in fact, resulting from bacteremia, viremia, hypoxia, chemical toxicity, or trauma [22].

Furthermore, it is common for there to be coagulopathy in the postoperative period, even if the patient does not present preoperatively, due to the extent of the liver resection. This complication is most noticeable, especially on the first and second days after surgery and can open the door for other complications related to bleeding. As an example, if the patient is using an epidural catheter to manage pain in the postoperative period, it should only be removed after normalization of coagulation parameters, as premature removal may result in vessel damage and consequent epidural hematomas [23,24].

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